

AGCAGAGAGCCTGGTGGGCATGGACATCTTTATCCACATACCTTAGTGTGAC
 CACGCCGACAGAAAATACTAAGGCCATCTCAGGGGTGCCTGTGCCAGGAGA
 GGGGGGCGGTGTCCCCGGGCGCAGAGCCATGCCTTTTCGGCCTGAAGCTCCG
 CAGGACTCGGCGCTACAACGTCCTGAGCAAGAACTGCTTTGTTGCCCGGATC
 CGCCTGCTGGACAGCAATGTCATCGAGTGCACGCTGTCGGTGGAAAGCACGG
 GGCAAGAGTGCCTGGAGGCCGTGGCCCAGAGGCTGGAGCTGAGGGGAGACGC
 ACTACTTCGGCCTTTTGTTTTCTCAGCAAGAGCCAGCAGGCGAGATGGGTTAGA
 GCTGGAGAAGCCACTGAAGAAACATCTGGACAAGTTTGCTAACGAGCCTCTG
 CTTTTCTTCGGAGTCATGTTCTATGTGCCAAATGTGTACACGGCTTCAGCAGGA
 GGCCACAAGATATCAGTATTACCTGCAAGTCAAAAAAGACGTGCTTGAAGGA
 CGGTTGCGGTGCTCCCTGGAACAAGTGATCCGGCTGGCTGGCTTAGCTGTGC
 AAGCTGACTTCGGAGATTATAACCAGTTTGATTCCCAAGAGTTCCTCCGAGA
 GTATGTGCTCTTTCCTATGGATTTGGCCATGGAGGAGGCGGCTCTGGAGGAG
 CTAACCCAGAAGGTGGCCCAGGAACACAAAGCTCATAGCGGGATCCTGCCG
 GCTGAAGCTGAAGTGTACATCAACGAGGTAGAGCGTTTGATGGATTG
 GACAGGAGATCTTCCCCGTGAAGGACAGTCATGGCAACAGCGTGACCTCGG
 CATCTTCTTCATGGGGATTTTGTGAGGAACAGGGTCGGGAGACAGGCAGTG
 ATATACAGGTGGAATGACATTGGGAGTGTTACTCACAGCAAAGCAGCCATCC
 TGTTGGAGCTGATTGACAAGGAGGAGACCGCGCTCTTCCATACAGATGATAT
 TGAAAATGCCAAGTACATTTCTCGGTTGTTTACCACTCGGCACAAATTTTACA
 AACAGAACAAGATCTGCACTGAACAGTCAAATTCTCCACCCCCAATCAGACG
 CCAGCCCACCTGGAGCCGGTCCTCACTGCCAAGGCAGCAGCCGTATATCTTG
 CCTCCCATGCATGTCCAGTGCACTGAGCACTACTCGGAGACCCATACTTCCCA
 AGACAGCATTTTCCCCGGGAACGAAGAAGCCTTGTACTGCCGTTCTCACAAAC
 AGCCTGGACCTTAATTACTTGAACGGCACCGTCACCAATGGCAGCGTGTGCA
 GCGTTCACAGCGTCAACTCCCTCAGCTGCTCCCAGAGCTTCATTCAGGCGTCT
 CCAGTGTCTCCAACCTTAGCATCCCTGGGAGTGACATCATGAGGGCCGATT
 ACATCCCCAGCCACCGCCACAGCACCATCATCGTGCCGTCTTACAGGCCGAC
 CCCAGATTACGAGACGGTCATGAGGCAGATGAAGAGGGGTCTGATGCACGC
 AGACAGCCAGAGCCGGTCTCTGCGTAACTCAATATCATCAACACCCATGCC
 TATAACCAGCCCGAGGAAGTGGTGTACAGCCAGCCGGAGATGCGGGAGAGG
 CATCCCTACACGGTCCCCTATGCACACCAGGGGTGCTACGGTCACAACTTG
 TAAGTCCGTCTGACCAGATGAACCCCCAAAATTGTGCGATGCCTATCAAGCC
 AGGGGCCAGTTCATCTCTCACACAGTGAGCACTCCAGAACTAGCCAACATG
 CAGCTCCAAGGAGCACAACTATAGCACAGCCCACATGCTCAAGAACTATC
 TATTCAGGCCGCCACCCCTTACCCTCGGCCCGTCCTGCCACCAGCACCCCA
 GACCTCGCCAGCCACCGCCACAAGTACGTCAGCGGCAGCAGCCCTGATCTGG
 TAACTCGGAAGGTGCAGCTCTCCGTAAAGACCTTCCAGGAGGACAGCTCACC
 TGTGGTCCATCAGTCTCTGCAGGAGGTGAGCGAACCCTCACAGCCACCAAG
 CACCATGGCGGCGGCGGTGGCACGGTGAATAAACGCCACAGCCTGGAGGTG

FIGURE 1A

ATGAACAGCATGGTGAGAGGCATGGAGGCCATGACACTGAAGTCACTCAATA
 TCCCCATGGCTCGCCGCAACACCCTTCGGGAGCAGGGCCCTTCCGAGGAGAC
 GGGCGGCCACGAAGTGCACGGTCTCCCCCAGTATCACCACAAGAAGACATTC
 TCGGATGCCACCATGCTGATCCACAGCAGTGAGAGCGAGGAAGAGGAGGAG
 ACCCTGGAGGCTGCACCTCAGGTTCTGTGCTTCGAGAGAAAGTAGAATACA
 GTGCCCAGCTGCAGGCTGCCCTGGCCCCGCATCCCCAACAGGCCCCCACCTGA
 GTACCCAGGGCCAAGAAAAAGTGTGAGTAATGGGGCACTGAGACAGGACCA
 GGGAAACCCCTCTTCTGCCATGGCCAGGTGCAGGGTGCTGAGACACGGACCA
 TCCAAGGCCCTCAGTGTCTCCCGGGCAGAGCAGCTGGCTGTCAACGGTGCCT
 CTCTGGGTCCCTCCATCTCTGAGCCTGACCTAACCAGCGTGAAGGAGCGGGT
 CAAGAAAGAGCCTGTGAAGGAAAGGCCGGTGTGAGAGATGTTCTCCCTGGAG
 GACAGCATTATAGAGAGAGAGATGATGATCAGGAATCTAGAGAAGCAGAAG
 ATGACGGGCCCCGCAGGCACAGAAGAGACCGCTGATGTTGGCAGCGCTGAAT
 GGGCTCTCGGTGGCCCGAGTGTGCGGGGCGGGAAGATGGTCGCCATGATGCCA
 CCCGAGTCCCCATAGACGAGAGGCTCAGAGCCCTGAAGAAGAAGCTGGAAG
 ATGGAATGGTGTTCACAGAATATGAGCAGATTCCAAACAAAAGGCCAACG
 GCGTCTTCAGCACCGCCACTCTGCCTGAGAACGCCGAGCGCAGCCGGATCCG
 AGAAGTTGTCCCATATGAGGAGAATCGAGTGGAGCTCATCCCGACCAAAGAA
 AACAAACACAGGCTATATCAACGCCTCCCACATCAAGGTGGTGGTCCGGCGGAT
 CAGAATGGCACTACATCGCCACCCAGGGGCCCTTGCCACATACGTGCCATGA
 CTTCTGGCAGATGGTGTGGGAGCAGGGGGTGAATGTGATCGCCATGGTCACT
 GCAGAGGAGGAGGGTGGACGGACCAAAAGCCATCGATACTGGCCCCAACTG
 GGGTCCAAGCATAGTTCTGCCACCTACGGCAAGTTCAAGGTCACCACAAAGT
 TCCGGACAGATTCTGGTTGCTATGCAACGACGGGCCCTAAAGGTGAAGCACCT
 GCTGTCCGGGCAGGAGAGGACCGTGTGGCACTTGACGTACACGGACTGGCCC
 CACCACGGCTGTCCAGAAGACGTCCAAGGATTTTTTGTCTACTTGGAGGAAA
 TCCAGTCAGTCCGACGCCACACCAACAGCGTGCTGGAAGGCATCAGGACCAG
 GCACCCCCCATCGTGGTTCCTGACGCGCGGGTGTGGGAAGGACTGGTGTG
 GTTATCCTCTCTGAGCTCATGATCTACTGCCTGGAACACAACGAAAAGGTGG
 AGGTGCCCACGATGCTGCGATTCTCAGGGAGCAGAGGATGTTTCATGATCCA
 GACCATTGCGCAGTACAAGTTCGTCTACCAAGTCCTCGTCCAGTTCCTGCAGA
 ATTCCAGGCTCATTTGATCTCCTCCGGGATGCAGCTTCTGGAGGAGGGACGC
 AGCTCTGTCTGACAGGGGGCGGCCACTTCGACAACATCTGCCTCCCCCAGCC
 AGAGGTGGATGGCTGGCAGCAGGCAGAAGCCAGAGTTACTCACAAACATCA
 TGTATTATTTTATATAAGATAATTTATTTTTTCCCTCTTTGGAATAAGTTCTG
 TGAGTTATTATATAATGCTTCCCCCCCCATACACACACAATAATATAGTGCT
 TCTCATTTG (SEQ ID NO:1)

FIGURE 1B

underlined = deleted in targeting construct

bold = sequence flanking Neo insert in targeting construct

AGCAGAGAGCCTGGTGGGCATGGACATCTTTATCCACATACCTTAGTGTGACCACGCCGA
 CAGAAACTACTAAGGCCATCTCAGGGGTGCTGTGCCAGGAGAGGGGGGCGGTGTCCCC
 GGGCCGCAGAGCCATGCCTTTCGGCCTGAAGCTCCGCAGGACTCGGCGCTACAACGTCTT
GAGCAAGAACTGCTTTGTTGCCCGGATCCGCCTGCTGGACAGCAATGTCATCGAGTGCAC
GCTGTCCGTGGAAAGCACGGGGCAAGAGTGCCTGGAGGCCGTGGCCCAGAGGCTGGAGCT
GAGGGAGACGCACCTACTTTCGGCCTTTGGTTTCTCAGCAAGAGCCAGCAGGCGAGATGGGT
 AGAGCTGGAGAAGCCACTGAAGAAACATCTGGACAAGTTTGCTAACGAGCCTCTGCTTTT
 CTTCCGAGTCATGTTCTATGTGCCAAATGTGTCACGGCTTCAGCAGGAGGCCACAAGATA
 TCAGTATTACCTGCAAGTCAAAAAAGACGTGCTTGAAGGACGGTTGCGGTGCTCCCTGGA
 ACAAGTGATCCGGCTGGCTGGCTTAGCTGTGCAAGCTGACTTCGGAGATTATAACCAGTT
 TGATTCCCAAGAGTTCCTCCGAGAGTATGTGCTCTTTCCTATGGATTTGGCCATGGAGGA
 GCGGCTCTGGAGGAGCTAACCCAGAAGGTGGCCCAGGAACACAAAGCTCATAGCGGGAT
 CCTGCCGGCTGAAGCTGAACTGATGTACATCAACGAGGTAGAGCGTTTGGATGGATTTGG
 ACAGGAGATCTTCCCCGTGAAGGACAGTCATGGCAACAGCGTGCACCTCGGCATCTTCTT
 CATGGGGATTTTTTGTGAGGAACAGGGTTCGGGAGACAGGCAGTGATATACAGGTGGAATGA
 CATTGGGAGTGTACTCACAGCAAAGCAGCCATCCTGTTGGAGCTGATTGACAAGGAGGA
 GACCGCTCTTCCATACAGATGATTTGAAAATGCCAAGTACATTTCTCGGTTGTTTAC
 CACTCGGCACAAATTTTACAAACAGAACAGATCTGCACTGAACAGTCAAATTTCTCCACC
 CCAATCAGACGCCAGCCACCTGGAGCCGGTCTCACTGCCAAGGCAGCAGCCGTATAT
 CTTGCCCTCCCATGCATGTCCAGTGCAGTGAGCACTACTCGGAGACCCATACTTCCCAAGA
 CAGCATTTTCCCCGGGAACGAAGAAGCCTTGTACTGCCGTTCTCACAACAGCCTGGACCT
 TAATTACTTGAACGGCACCGTCAACCAATGGCAGCGTGTGCAGCGTTCACAGCGTCAACTC
 CCTCAGCTGCTCCAGAGCTTCATTACAGGCGTCTCCAGTGTCTCCAACCTTAGCATCCC
 TGGGAGTGACATCATGAGGGCCGATTACATCCCCAGCCACCGCCACAGCACCATCATCGT
 GCCGTCTTACAGGCCGACCCAGATTACGAGACGGTCATGAGGCAGATGAAGAGGGGTCT
 GATGCACGCAGACAGCCAGAGCCGGTCTCTGCGTAACCTCAATATCATCAACACCCATGC
 CTATAACCAGCCCCGAGGAACCTGGTGTACAGCCAGCCGGAGATGCGGGAGAGGCATCCCTA
 CACGGTCCCCTATGCACACCAGGGGTGCTACGGTCACAAACTTGTAAGTCCGTCTGACCA
 GATGAACCCCCAAAATTGTGCGATGCCATCAAGCCAGGGGCCAGTTCCATCTCTCACAC
 AGTGAGCACTCCAGAACTAGCCAACATGCAGCTCCAAGGAGCACAACTATAGCACAGC
 CCACATGCTCAAGAACTATCTATTACAGGCCGCCACCCCTTACCCTCGGCCCGTCTCTGC
 CACCAGCACCCAGACCTCGCCAGCCACCGCCACAAGTACGTCAGCGGCAGCAGCCCTGA
 TCTGGTAACTCGGAAGGTGCAGCTCTCCGTAAAGACCTTCCAGGAGGACAGCTCACCTGT
 GGTCCATCAGTCTCTGCAGGAGGTGAGCGAACCCCTCACAGCCACCAAGCACCATGGCGG
 CGGCGGTGGCACGGTGAATAAACGCCACAGCCTGGAGGTGATGAACAGCATGGTGAGAGG
 CATGGAGGCCATGACACTGAAGTCACTCAATATCCCCATGGCTCGCCGCAACACCCCTCG
 GGAGCAGGGCCCTTCCGAGGAGACGGGCGGCCACGAAGTGCACGGTCTCCCCCAGTATCA
 CCACAAGAAGACATTCTCGGATGCCACCATGCTGATCCACAGCAGTGAGAGCGAGGAAGA

FIGURE 2A

GGAGGAGACCCTGGAGGCTGCACCTCAGGTTCCCTGTGCTTCGAGAGAAAGTAGAATACAG
 TGCCCAGCTGCAGGCTGCCCTGGCCCCGCATCCCCAACAGGCCCCACCTGAGTACCCAGG
 GCCAAGAAAAAGTGTCTAGTAATGGGGCACTGAGACAGGACCAGGGAACCCCTCTTCCTGC
 CATGGCCAGGTGCAGGGTGTGAGACACGGACCATCCAAGGCCCTCAGTGTCTCCCGGGC
 AGAGCAGCTGGCTGTCAACGGTGCCTCTCTGGGTCCCTCCATCTCTGAGCCTGACCTAAC
 CAGCGTGAAGGAGCGGGTCAAGAAAGAGCCTGTGAAGAAAGGCCGGTGTGAGAGATGTT
 CTCCTGGAGGACAGCATTATAGAGAGAGAGATGATGATCAGGAATCTAGAGAAGCAGAA
 GATGACGGGCCCCGAGGCACAGAAGAGACCGCTGATGTTGGCAGCGCTGAATGGGCTCTC
 GGTGGCCCCGAGTGTGCGGGCGGGAAGATGGTCGCCATGATGCCACCCGAGTCCCCATAGA
 CGAGAGGCTCAGAGCCCTGAAGAAGAAGCTGGAAGATGGAATGGTGTTCACAGAATATGA
 GCAGATTCCAAACAAAAAGGCCAACGGCGTCTTCAGCACCGCCACTCTGCCTGAGAACGC
 CGAGCGCAGCCGGATCCGAGAAGTTGTCCCATATGAGGAGAATCGAGTGGAGCTCATCCC
 GACCAAAGAAAAACAACACAGGCTATATCAACGCCTCCACATCAAGGTGGTGGTTCGGCGG
 ATCAGAATGGCACTACATCGCCACCCAGGGGCCCTTGCCACATACGTGCCATGACTTCTG
 GCAGATGGTGTGGGAGCAGGGGGTGAATGTGATCGCCATGGTCACTGCAGAGGAGGAGGG
 TGGACGGACCAAAGCCATCGATACTGGCCCAAAGTGGGGTCCAAGCATAGTTCTGCCAC
 CTACGGCAAGTTCAAGGTCACCACAAAGTTCCGGACAGATTCTGGTTGCTATGCAACGAC
 GGGCCTAAAGGTGAAGCACCTGCTGTCCGGGCAGGAGAGGACCGTGTGGCACTTGCAGTA
 CACGGACTGGCCCCACCACGGCTGTCCAGAAGACGTCCAAGGATTTTTGTCTACTTGGA
 GGAAATCCAGTCAGTCCGACGCCACACCAACAGCGTGTGGAAGGCATCAGGACCAGGCA
 CCCCCCATCGTGGTTCACTGCAGCGCGGGTGTGGGAAGGACTGGTGTGGTTATCCTCTC
 TGAGCTCATGATCTACTGCCTGGAACACAACGAAAAGGTGGAGGTGCCACGATGCTGCG
 ATTCCTCAGGGAGCAGAGGATGTTTCATGATCCAGACCATTCGCGAGTACAAGTTTCGTCTA
 CCAAGTCCTCGTCCAGTTCCTGCAGAATTCCAGGCTCATTTGATCTCCTCCGGGATGCAG
 CTTCTGGAGGAGGGACGCAGCTCTGTCCTGCAGGGGGCGGCCACTTCGACAACATCTGCC
 TCCCCCAGCCAGAGGTGGATGGCTGGCAGCAGGCAGAAGCCAGAGTTACTCACAAACATC
 ATGTATTATTTTATATAAGATAATTTATTTTTTTCCCTCTTTGGAATAAGTTCTGTGAGT
 TATTATATAATGCTTCCCCCCCCATACACACACAATAATATAGTGCTTCTCATTTG

FIGURE 2B

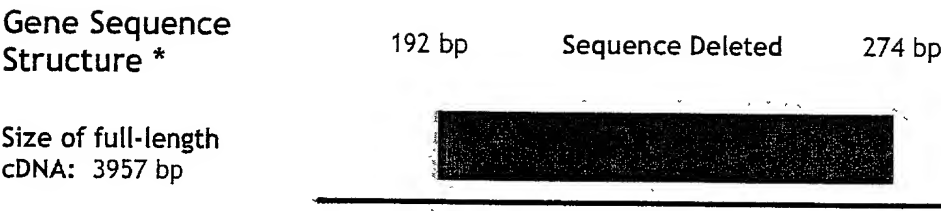
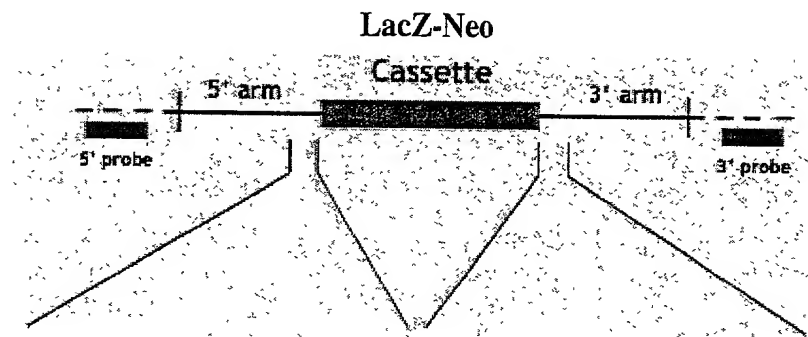


FIGURE 3

Targeting Vector*
(genomic sequence)

Arm Length:
5': 3.5 kb
3': 2 kb



Targeting Vector
Endogenous Locus

* Not drawn to scale

5'>CAGCTGCCCCGGCAGAGAGCCT GGTGGGCATGGACATCTTTATCCA CATACCTTAGTGTGACCACGCCGA CAGAAACTACTAAGGCCATCTCA GGGGTGCCCTGTGCCAGGAGAGGGG GGCGGTGTCCCCGGGCCGAGAGC CATGCCTTTCGGCCTGAAGCTCCG CAGGACTCGGCGCTACAACGTCCT GAGCAAGAACT<3' (SEQ ID NO:2)	5'>GAGGCCGTGGCCCAGAGGCTG GAGCTGAGGGAGGTGAGTTGAGCG CGCATCCCTGCCTGTTGTGTGGAC AGGGAGTGGGCTCTTCAGAGGAAC CAGCTATCTGCTTAACGTGTTGGC ACCTGCTGTGTTTTTCAGCCTAAGC GTGTGTTTAAAAGAACCTGCTTTT CTTAGGGTGGGTGTGGCCCCGGGA AGTTCCAGCAT<3' (SEQ ID NO:3)
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FIGURE 4